**Amendments to the Specification:**

Please replace the heading and paragraph immediately after the title (page 1, lines 1 and 2) with the following redlined heading and paragraph:

-- CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims the benefit of priority from U.S. Application No. 60/168,976, filed December 3, 1999, now abandoned, and U.S. Application No. 60/137,900, filed June 7, 1999, now abandoned. ~~All prior applications are incorporated herein by reference.~~ --

Please replace the paragraph beginning at page 4, line 19, with the following redlined paragraph:

-- Figure 2 is a schematic representation of a single chain antibody-genomic streptavidin fusion construct. Shown is the scFV gene consisting of variable regions of the light ($V_l$) and heavy ($V_h$) chains separated by the linker $(Gly_4Ser)_3$ (SEQ ID NO:10). Streptavidin (amino acids 25-183 of SEQ ID NO:2) is joined to the 3' terminus of the scFV gene separated by a second linker, GSGSA (SEQ ID NO:48). --

Please replace the paragraph beginning at page 6, line 18, with the following redlined paragraph:

-- The genomic streptavidin molecules of the subject invention also include variants (including alleles) of the native protein sequence. Briefly, such variants may result from natural polymorphisms or may be synthesized by recombinant DNA methodology, and differ from wild-type protein by one or more amino acid substitutions, insertions, deletions, or the like. Variants generally have at least 75% nucleotide identity to native sequence, preferably at least 80%-85%, and most preferably at least 90% nucleotide identity. Typically, when engineered, amino acid substitutions will be conservative, *i.e.*, substitution of amino acids within groups of polar, non-polar, aromatic, charged, etc. amino acids. With respect to homology to the native sequence, variants should preferably have at least 90% amino acid sequence identity, and within certain embodiments, greater than 92%, 95%, or 97% identity. Such amino acid sequence

identity may be determined by standard methodologies, including use of the National Center for Biotechnology Information BLAST search methodology ~~available at www.ncbi.nlm.gov using default parameters~~. The identity methodologies most preferred are those described in U.S. Patent 5,691,179 and Altschul *et al.*, *Nucleic Acids Res. 25*:3389-3402, 1997. --

Please replace the paragraph beginning at page 11, line 28, with the following redlined paragraph:

-- In addition to a cloning site, the cassette may include a linker molecule. Linker molecules are typically utilized within the context of fusion proteins and are well known in the art. As exemplified in Figure 2, linkers are typically utilized to separate the genomic streptavidin sequence from the other sequences linked thereto and to separate the $V_H$ and the $V_L$ of the scFV. The linking sequence can encode a short peptide or can encode a longer polypeptide. Preferable linker sequences encode at least two amino acids, but may encode as many amino acids as desired as long as functional activity is retained. In the various embodiments, the linker sequence encodes 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, and 35 amino acids. In certain embodiments an encoded linker may be a standard linker such as $(Gly_4Ser)_x$ (SEQ ID NO:47) where x may be any integer, but is preferably 1 to 10. The length and composition can be empirically determined to give the optimum expression and biochemical characteristics. For example, the composition of the linker can be changed to raise or lower the isoelectric point of the molecule. Additionally, one of ordinary skill in the art will appreciate that the length of linker between variable light and heavy chains need be at least long enough to facilitate association between the two domains, while the linker between streptavidin and the antibody fragment may vary from zero amino acids to 100 or more as long as functionality is maintained. Accordingly, the linker between the light and heavy chain is typically greater than five amino acids, and preferably greater than ten, and more preferably greater than fifteen amino acids in length. --

Please replace the paragraph beginning at page 18, line 24, with the following redlined paragraph:

-- Once the variable light ($V_L$) and heavy chain ($V_H$) DNA is obtained, the sequences may be ligated together, either directly or through a DNA sequence encoding a peptide linker, using techniques well known to those of skill in the art. In a preferred embodiment, heavy and light chain regions are connected by a flexible polypeptide linker (*e.g.*, $(Gly_4Ser)_x$ [SEQ ID NO:47, where x may be any integer, but is preferably 1 to 10, described *supra*], or the pKOD sequence, or others, such as those provided, *infra*) which starts at the carboxyl end of the light chain Fv domain and ends at the amino terminus of the heavy chain Fv domain, or vice versa, as the order of the Fv domains can be either light-heavy or heavy-light. The entire sequence encodes the Fv domain in the form of a single-chain antigen binding protein. --

Please replace the paragraph beginning at page 19, line 21, with the following redlined paragraph:

-- Accordingly, once a DNA sequence has been identified that encodes an Fv region which when expressed shows specific binding activity, fusion proteins comprising that Fv region may be prepared by methods known to one of skill in the art. The Fv region may be fused to genomic streptavidin directly in the expression cassette of the present invention or, alternatively, may be joined directly to genomic streptavidin through a peptide or polypeptide linker, thereby forming a linked product. The linker may be present simply to provide space between the Fv and the fused genomic streptavidin or to facilitate mobility between these regions to enable them to each attain their optimum conformation. The genomic streptavidin-antibody expression cassette, typically, comprises a single vector which provides for the expression of both heavy and light variable sequences fused by an appropriate linker as well as a linker fusing the light and heavy chains with genomic streptavidin, thereby encoding a single chain antibody:genomic streptavidin (scFvSA) conjugate. In one embodiment the linker connecting the variable light and heavy chains is of sufficient length or side group selection to allow for flexibility. In one embodiment the linker is a standard linker such as $(Gly_4Ser)_x$ [SEQ ID NO:47,

where x may be any integer, but is preferably 1 to 10], described *supra*, while in another embodiment the linker is the pKOD linker (GlyLeuGluGlySerProGluAlaGlyLeuSerProAspAlaGlySerGlySer) (SEQ ID NO: 9). It should be understood that a variety of linkers may be used, but in some embodiments it may be preferred that the linker separating the light and heavy antibody chains should allow flexibility and the linker attaching the scFv to the genomic streptavidin sequence can be fairly rigid or fairly flexible. Further, in addition to linkers, additional amino acids may be encoded by the addition of restriction sites to facilitate linker insertion and related recombinant DNA manipulation, as such these amino acids while not necessarily intended to be linkers may or may not be included within the constructs described herein, depending on the construction method utilized. --

Please replace the paragraph beginning at page 29, line 30, with the following redlined paragraph:

-- The streptavidin and huNR-LU-10 scFv genes (a monoclonal antibody that binds the antigen EGP40 or EPCAM, epithelial glycoprotein, 40 kD) were cloned onto separate plasmids prior to construction of the huNR-LU-10 scFvSA gene. The streptavidin gene, signal sequence and approximately 300 bp of upstream sequence were PCR-amplified from *Streptomyces avidinii* (ATCC 27419) genomic DNA and cloned into pEX-1 as an *EcoRI/HindIII* fragment to form pEX318 (Figure 7). The huNR-LU-10 scFv was derived from the humanized antibody plasmid pNRX451 (Graves *et al., Clin. Cancer Res., 5*:899-908, 1999). The heavy and light chain variable regions were PCR-amplified separately from pNRX451 and then combined in a subsequent PCR. Oligonucleotides used in this process were designed to introduce a $(Gly_4Ser)_3$ linker (SEQ ID NO:10) between the leading $V_L$ and the trailing $V_H$. The resulting PCR product was cloned into pEX-1 as a *NcoI/HindIII* fragment forming the plasmid pEX-scFv3.2.1 (Figure 7). The scFv and streptavidin genes were PCR-amplified from pEX-scFv3.2.1 and pEX318, respectively, and combined into a fusion, as illustrated in Figure 8. The oligonucleotides used in these reactions created an overlap between the 3' end of the leading scFv and the 5' end of the trailing streptavidin, which encoded a five amino acid linker (GSGSA; SEQ ID NO:48). The fragments were joined by PCR using the outside primers. The resulting

1.25 kb fragment was cloned into the *NdeI* and *BamHI* sites of vector pET3a (Novagen), generating pET3a-41B. This plasmid was digested with *XhoI* and *HindIII*, and the 1.3 kb fragment containing the $V_H$-SA coding region and transcription terminator was ligated to a 4.6 kb *XhoI/HindIII* fragment of pEX-scFv3.2.1 containing the $V_L$ coding region, *lac* promoter, and ampicillin resistance gene (pYL256). The streptavidin regulatory region and signal sequence were PCR-amplified from pEX318 and cloned into the *EcoRI/NcoI* sites of pYL256 to form pEX94B (Figure 8). --

Please replace the paragraph beginning at page 34, line 33, with the following redlined paragraph:

-- Clones were further grown in an 8L fermentor and analyzed for expression level. The primary inoculum (50 ml) was grown overnight at 30°C in shake flasks containing Terrific broth plus 50 μg/ml kanamycin (plasmids pEX94Bneo or E31-2-20) or carbenicillin (plasmids pEX94B or E5-2-6), depending on the selectable marker of the plasmid. The culture was then diluted 100-fold into the same medium and grown at 30°C for an additional 4-5 h. This secondary inoculum (0.5 liter) was transferred to a 14 liter ~~BioFlo~~ BIOFLO 3000 fermentor (New Brunswick Scientific) containing 8 liters of complete *E. coli* medium [per liter: 6 g $Na_2HPO_4$, 3 g $KH_2PO_4$, 0.5 g NaCl, 3 g $(NH_4)_2SO_4$, 48 g yeast extract (Difco), 0.25 ml ~~Mazu~~ MAZU DF204 antifoam (PPG Industries Inc., Pittsburgh, PA), 0.79 g $MgSO_4$ -$7H_2O$, 0.044 g $CaCl_2$-$2H_20$, and 3 ml of trace elements (per liter: 0.23 g $CoCl_2$, 0.57 g $H_3BO_3$, 0.2 g $CuCl_2$-$2H_2O$, 3.5 g $FeCl_3$-$6H_2O$, 4.0 g $MnCl_2$-$4H_2O$, 0.5 g ZnCl, 1.35 g thiamine, and 0.5 g $Na_2MoO_4$-$2H_2O$)]. The medium contained an initial 5 g/liter galactose as carbon source plus 50 μg/ml of kanamycin or carbenicillin for plasmid retention. The culture was grown at 30°C and induced with IPTG (0.2 mM) at 6 h post-inoculation. The pH was maintained at 7.0 by the automatic addition of either phosphoric acid or NaOH. Dissolved oxygen concentration was maintained at or above 30% throughout the run using agitation speeds of 400-800 rpm and oxygen supplementation as necessary. A galactose solution (50%) was fed over a 9 h period after exhaustion of the initial galactose present in the medium to a total of 20-25 g per liter. Cells were harvested at 24-26 h post-inoculation (for B9E9 scFvSA) or 48-56 h post-inoculation (for

huNR-LU-10 scFvSA) in a continuous flow centrifuge (~~Pilot Powerfuge~~POWERFUGE PILOT, Carr Separations, Franklin, MA), washed with PBS (10 mM sodium phosphate, 150 mM NaCl, pH 7.2), and pelleted by centrifugation. A typical fermentation produced 80-90 g of cells (wet wt) per liter culture medium. --

Please replace the paragraph beginning at page 36, line 4, with the following redlined paragraph:

-- Alternatively, a rhodamine-biotin HPLC assay was devised that provided faster results. The fusion protein in centrifuged lysates was complexed with excess rhodamine-derivatized biotin, which was prepared as follows: 5-(and-6-)-carboxytetramethylrhodamine, succinimidyl ester (Molecular Probes, Eugene OR) was coupled to biocytin (Pierce, Rockford IL) through the formation of a stable amide bond. The reaction mixture was purified by HPLC using a ~~Dynamax~~ DYNAMAX semi-preparative C-18 column (Rainin Instrument Co., Woburn, MA). The effluent was monitored at 547 nm and peak fractions collected and analyzed by mass spectrometry. Fractions corresponding in molecular weight to biocytin-rhodamine conjugate were pooled and concentrated by roto-evaporation (Buchii, Switzerland). An excess of purified biocytin-rhodamine conjugate was added to the clarified crude lysate and analyzed by size exclusion chromatography using a ~~Zorbax~~ ZORBAX GF-250 column (MAC-MOD, Chadds Ford PA) equilibrated in 20 mM sodium phosphate containing 15% DMSO at 1.0 ml/min flow rate. The effluent was monitored at 547 nm using a Varian ~~Dynamax~~ DYNAMAX PDA-2 detector, and the peak area corresponding to fusion protein elution was determined using a Varian Dynamax HPLC Data System (Walnut Creek, CA). The concentration of fusion protein in the crude lysate was calculated by comparison to a standard analyzed under the same conditions. The molar extinction coefficient for the fusion protein standard was calculated using a previously described method summing the relative contributions of amino acids absorbing at 280 nm (Gill and von Hippel, *Analyt. Chem. 182*:319-326, 1989). --

Please replace the paragraph beginning at page 37, line 5, with the following redlined paragraph:

-- A number of genetic variants were constructed that contained linkers of different lengths and composition and the variable regions in different order (Table 1). These constructs were initially grown and induced in shake flask cultures and qualitatively assessed for expression by visualizing periplasmic proteins on Coomassie-stained, non-reducing SDS gels. High-expressing constructs were further tested in an 8L fermentor using a galactose fed-batch protocol, and their expression levels were quantitatively determined by size exclusion HPLC using rhodamine-derivatized biotin. The construct that best fulfilled these criteria contained a 25-mer $Gly_4Ser$ linker (SEQ ID NO:11) with the scFv in the $V_HV_L$ orientation. --

Please replace the paragraph beginning at page 38, line 13, with the following redlined paragraph:

In order to clone the DNA fragment of the *fkpA* gene, chromosomal DNA was extracted from *E. coli* XL1-Blue cells (Stratagene) and digested with *Xho*I. Thirty-five cycles of PCR were performed using a pair of oligonucleotides (RX1229: ACGACGGTTGCTGCGGCGGTC (SEQ ID NO: 32); RX1231: AGGCTCATTAAT GATGCGGGT (SEQ ID NO: 33); both obtained from Operon Technologies, Inc.) and 300 ng of the digested genomic DNA as a template. The PCR mixture was subject to a second round of PCR (30 cycles) using a pair of nested oligonucleotides (RX1230: GGATCCAAGCTTACGATCACGGTCATGAACACG (SEQ ID NO: 34); RX1232: CTCGAGAAGCTTTAACTAAATTAATACAGCGGA) (SEQ ID NO: 35). The PCR fragments were resolved on a 1% agarose gel, and the 1.6-kb fragment was isolated. The extracted DNA was cloned into the TA vector (Invitrogen), and the sequence was confirmed by DNA sequencing. The clone was digested with *Hind*III, using a site that was incorporated into oligonucleotides RX1230 and RX 1232 and was ligated with *Hind*III-digested vector E84-2-8 (NeoRx Corp.), harboring the anti-CEA T84.66 scFvSA fusion gene (T84.66 cDNA from City of Hope, Duarte, CA). The resultant plasmid (F115-1-1) was used to transform XL1-Blue *E. coli* for shake-flask expression. The periplasmic components were extracted and analyzed on 4-20%

SDS-PAGE. For electrophoretic analysis, 20 µl of the solution of scFvSA periplasmic fusion proteins were loaded in each lane of the gel. Following electrophoresis, the gel was stained with Coomassie Blue R250. The FkpA protein, with a molecular weight of about 30,000, was prominently present in all samples carrying the *fkpA* gene (+), while absent in those lacking the gene (-), as shown, for example, in Figure 19. The molecular weights of the seven components in the ~~SeeBlue~~ SEEBLUE molecular standard marker (M), obtained from Novex, listed in order of increasing size, from the bottom of the gel, are 16,000; 30,000; 36,000; 50,000; 64,000; 98,000; and 250,000. As seen in Figure 19, expression of the T84.66 scFvSA fusion protein increased dramatically when co-expressed with the FkpA chaperone protein, in comparison to the parent construct (E84-2-8) lacking the *fkpA* gene. Additional scFvSA fusions were constructed by moving *Nco*I-*Sac*I fragments to the F115-1-1 vector, which had previously been restricted with *Nco*I and *Sac*I. The resultant plasmids were tested in *E. coli* XL1-Blue shake flask cultures. Upon electrophoretic analysis, several showed increased fusion protein expression, as demonstrated in Figure 19 and Table 2. The results summarized here involve only the $V_h$-$V_l$-SA fusion configuration incorporating the $(Gly_4Ser)_5$ (SEQ ID NO: 11)linker. As summarized in Table 2, the expression levels of fusion proteins in the shake flask experiments were estimated qualitatively, with the highest level assigned a level of +++++. --

Please replace the paragraph beginning at page 42, line 1, with the following redlined paragraph:

-- SDS-PAGE demonstrated that the fusion proteins were purified to > 95% homogeneity after iminobiotin chromatography (Figure 12, lanes 2 & 3; huNR-LU-10 data only). The major band migrated at the expected molecular weight of ~173 kDa with minor isoforms evident. These isoforms were also detected with polyclonal anti-streptavidin antibody on Western gel analysis (data not shown). However, all bands resolved into a single species of ~ 43 kDa when the protein was boiled prior to electrophoresis, consistent with a single protein entity dissociable into its homogeneous subunit (Figure 12, lanes 4 & 5). The molecular weights of the seven components in the ~~SeeBlue~~ SEEBLUE molecular standard marker (Figure 12, lane 1), available from Novex, are described in Example V. --

Please replace the paragraph beginning at page 42, line 12, with the following redlined paragraph:

-- ***Size exclusion HPLC and Laser Light Scattering Analysis.*** Purified protein preparations were analyzed by size exclusion HPLC performed on a ~~Zorbax~~ ZORBAX GF-250 column with a 20 mM sodium phosphate/0.5 M NaCl mobile phase. The molecular weight of the fusion construct was measured using this ~~Zorbax~~ ZORBAX system connected in series with a Varian Star 9040 refractive index detector and a MiniDawn light scattering instrument (Wyatt Technologies, Santa Barbara, CA). A dn/dc value of 0.185 for a protein in an aqueous buffer solution was used in the molecular weight calculations. --

Please replace the paragraph beginning at page 42, line 27, with the following redlined paragraph:

-- ***Amino-terminal sequencing.*** Automated amino acid sequencing was performed using a ~~Procise~~ PROCISE 494 sequenator (Applied Biosystems, Inc., Foster City, CA). This revealed that the leader sequences of both huNR-LU-10 scFvSA and B9E9 scFvSA were cleaved at the expected signal peptidase site adjacent to the first amino acid of the variable region. --

Please delete the section of the specification entitled "Sequence Listing" beginning immediately after the section of the specification entitled "Abstract of the Disclosure" on page 58, and insert the enclosed Sequence Listing therefore.